Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

DABCO as a Practical Catalyst for Aromatic Halogenation with *N*-Halosuccinimides

Haiyan Xu,[a] Lanping Hu,[b] Guanghua Zhu,[b] Yueping Zhu,[a] Yang Wang,[b] Zhengguang Wu,[b] You Zi *[b] and Weichun Huang*[b]

[a] Nantong Normal College, Nantong 226010, Jiangsu, China
[b] School of Chemistry and Chemical Engineering, Nantong University
Nantong 226019, Jiangsu, P. R. China.

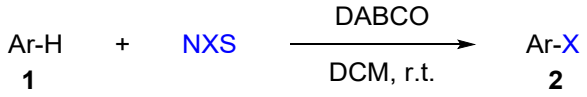
*E-mail: ziyou@ntu.edu.cn; huangweichun@ntu.edu.cn

Contents

General remarks

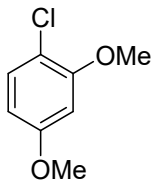
All the chemicals that are not mentioned in the subsequent parts were purchased from Rhawn, Energy Chemical, Aladdin, Macklin or TCI and used without further purification. For column chromatography, flash column and TLC (SiO2, 60M, pore size 0.04 – 0.063 mm) were used. The TLC-glass-plates consisted of a 0.25 mm layer of silica 60 with Fluorescence indicator UV254. TLCs were checked under UV-light (254 nm or 365 nm) and stained with an aq. KMnO4-solution. All ^{1}H, ^{13}C NMR spectra were measured with a BRUKER Avance 400 spectrometer. The chemical shift of each signal was registered in ppm. For ^{1}H and ^{13}C measurements, the chemical shift refers to TMS, showing a signal at 0 ppm. As an internal standard, the remaining protons or respectively the carbons of the corresponding deuterated solvent were used ($CDCl_3$, 7.26 ppm (^{1}H-NMR), 77.16 ppm (^{13}C-NMR)). High-resolution mass spectra (HRMS) were measured with EI or ESI ionisation by the MS plattform. A chromatographic purification was performed before each measurement.

Synthesis of Aromatic halides



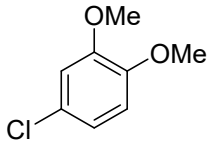
To an oven dried round bottom flask equipped with a stirring bar was charged with the arene/heterocyce (0.5 mmol, 1.0 eq.), *N*-halosuccinimide (1.1 eq.) and DABCO (5 mol%). DCM (2 ml) was added and the reaction vessel was sealed and stirred at ambient temperature. The reaction was stopped when it completed, monitored by TLC. The crude product was purified by column chromatography using silica gel with ethyl acetate in petroleum ether as the eluent.

1-Chloro-2,4-dimethoxybenzene (2a) [1]



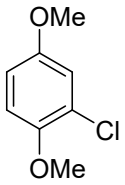
Yield: 93%, colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 (d, *J* = 8.6 Hz, 1H), 6.50 (d, *J* = 2.7 Hz, 1H), 6.42 (dd, *J* = 8.7, 2.7 Hz, 1H), 3.86 (s, 3H), 3.78 (s, 3H).

4-Chloro-1,2-dimethoxybenzene (2b) [1]



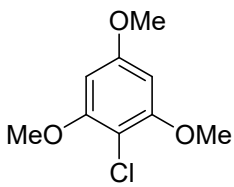
Yield: 96%, colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.90 – 6.82 (m, 2H), 6.76 (d, *J* = 8.5 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H).

2-Chloro-1,4-dimethoxybenzene (2c) [1]



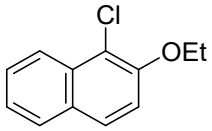
Yield: 95%, colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.96 (d, *J* = 3.0 Hz, 1H), 6.89 – 6.83 (m, 1H), 6.77 (dd, *J* = 9.0, 3.0 Hz, 1H), 3.85 (s, 3H), 3.76 (s, 3H).

2-Chloro-1,3,5-trimethoxybenzene (2d) [2]



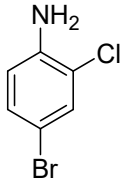
Yield: 98%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.19 (s, 2H), 3.88 (s, 6H), 3.82 (s, 3H).

1-Chloro-2-ethoxynaphthalene (2e) [3]



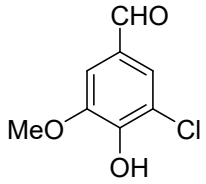
Yield: 99%, pale brown solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 (d, *J* = 8.6 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 9.0 Hz, 1H), 7.56 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 7.40 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 7.29 (d, *J* = 9.0 Hz, 1H), 4.27 (q, *J* = 7.0 Hz, 2H), 1.51 (t, *J* = 7.0 Hz, 3H).

4-Bromo-2-chloroaniline (2f) [4]



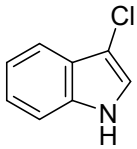
Yield: 60%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (d, *J* = 2.3 Hz, 1H), 7.16 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.64 (d, *J* = 8.6 Hz, 1H), 4.04 (s, 2H).

3-Chloro-4-hydroxy-5-methoxybenzaldehyde (2g) [1]



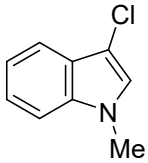
Yield: 53%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.79 (s, 1H), 7.50 (d, *J* = 1.7 Hz, 1H), 7.34 (d, *J* = 1.7 Hz, 1H), 6.44 (s, 1H), 3.99 (s, 3H).

3-Chloro-1H-indole (2j) [5]



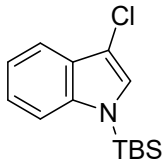
Yield: 92%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 (s, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.20 – 7.12 (m, 2H), 7.10 (d, *J* = 2.6 Hz, 1H).

3-Chloro-1-methyl-1H-indole (2k) [2]



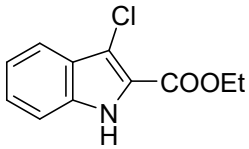
Yield: 79%, pale yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 7.9 Hz, 1H), 7.35 – 7.27 (m, 2H), 7.21 (ddd, *J* = 8.0, 6.3, 1.8 Hz, 1H), 7.03 (s, 1H), 3.76 (s, 3H).

1-(^{t}Butyldimethylsilyl)-3-chloro-1H-indole (2l) [2]



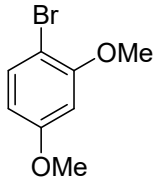
Yield: 63%, pale brown liquid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.62 (m, 1H), 7.53 – 7.48 (m, 1H), 7.25 – 7.18 (m, 2H), 7.15 (s, 1H), 0.96 (s, 9H), 0.62 (s, 6H).

Ethyl 3-chloro-1H-indole-2-carboxylate (2m) [1]



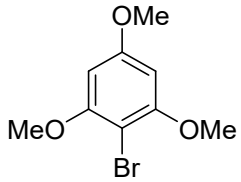
Yield: 87%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.94 (s, 1H), 7.72 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.42 – 7.35 (m, 2H), 7.23 (ddd, *J* = 8.0, 5.7, 2.2 Hz, 1H), 4.47 (q, *J* = 7.1 Hz, 2H), 1.46 (t, *J* = 7.1 Hz, 3H).

1-Bromo-2,4-dimethoxybenzene (2n) [6]



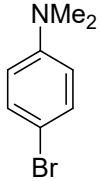
Yield: 89%, colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 8.7 Hz, 1H), 6.48 (d, *J* = 2.7 Hz, 1H), 6.39 (dd, *J* = 8.7, 2.8 Hz, 1H), 3.86 (s, 3H), 3.79 (s, 3H).

2-Bromo-1,3,5-trimethoxybenzene (2o) [4]



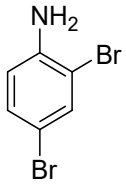
Yield: 99%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.18 (s, 2H), 3.88 (s, 6H), 3.82 (s, 3H).

4-Bromo-N,N-dimethylaniline (2p) [8]



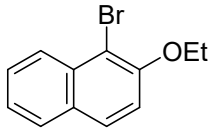
Yield: 65%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 – 7.16 (m, 2H), 6.57 – 6.36 (m, 2H), 2.83 (s, 6H).

2,4-Dibromoaniline (2q) [4]



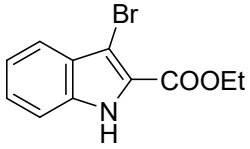
Yield: 83%, brown solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 2.2 Hz, 1H), 7.19 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.64 (d, *J* = 8.6 Hz, 1H), 4.10 (s, 2H).

1-Bromo-2-ethoxynaphthalene (2r) [7]



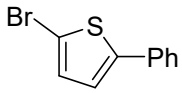
Yield: 98%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.24 (dd, *J* = 8.6, 1.0 Hz, 1H), 7.83 – 7.77 (m, 2H), 7.57 (ddd, *J* = 8.5, 6.8, 1.3 Hz, 1H), 7.41 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.28 (d, *J* = 3.5 Hz, 1H), 4.28 (q, *J* = 7.0 Hz, 2H), 1.54 (t, *J* = 7.0 Hz, 3H).

Ethyl 3-bromo-1H-indole-2-carboxylate (2s) [9]



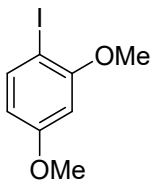
Yield: 85%, pale yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.03 (s, 1H), 7.68 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.44 – 7.33 (m, 2H), 7.23 (s, 1H), 4.46 (d, *J* = 7.2 Hz, 2H), 1.46 (s, 3H).

2-Bromo-5-phenylthiophene (2t) [10]



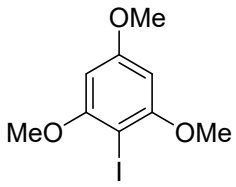
Yield: 98%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 – 7.49 (m, 2H), 7.38 (s, 2H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.04 (d, *J* = 5.7 Hz, 2H).

1-Iodo-2,4-dimethoxybenzene (2u) [6]



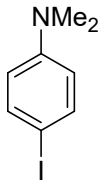
Yield: 69%, colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.6 Hz, 1H), 6.43 (d, *J* = 2.6 Hz, 1H), 6.32 (dd, *J* = 8.6, 2.7 Hz, 1H), 3.85 (s, 3H), 3.79 (s, 3H).

2-Iodo-1,3,5-trimethoxybenzene (2v) [4]



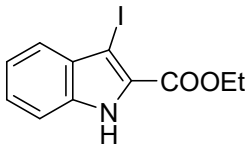
Yield: 98%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.15 (s, 2H), 3.87 (s, 6H), 3.83 (s, 3H).

4-Iodo-N,N-dimethylaniline (2w) [11]



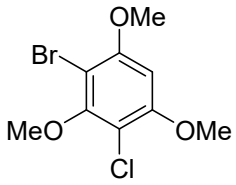
Yield: 95%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (d, *J* = 8.9 Hz, 2H), 6.49 (d, *J* = 8.9 Hz, 2H), 2.92 (s, 6H).

Ethyl 3-iodo-1H-indole-2-carboxylate (2x) [4]



Yield: 94%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.18 (s, 1H), 7.62 – 7.55 (m, 1H), 7.41 – 7.34 (m, 2H), 7.26 – 7.20 (m, 1H), 4.47 (q, *J* = 7.1 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H).

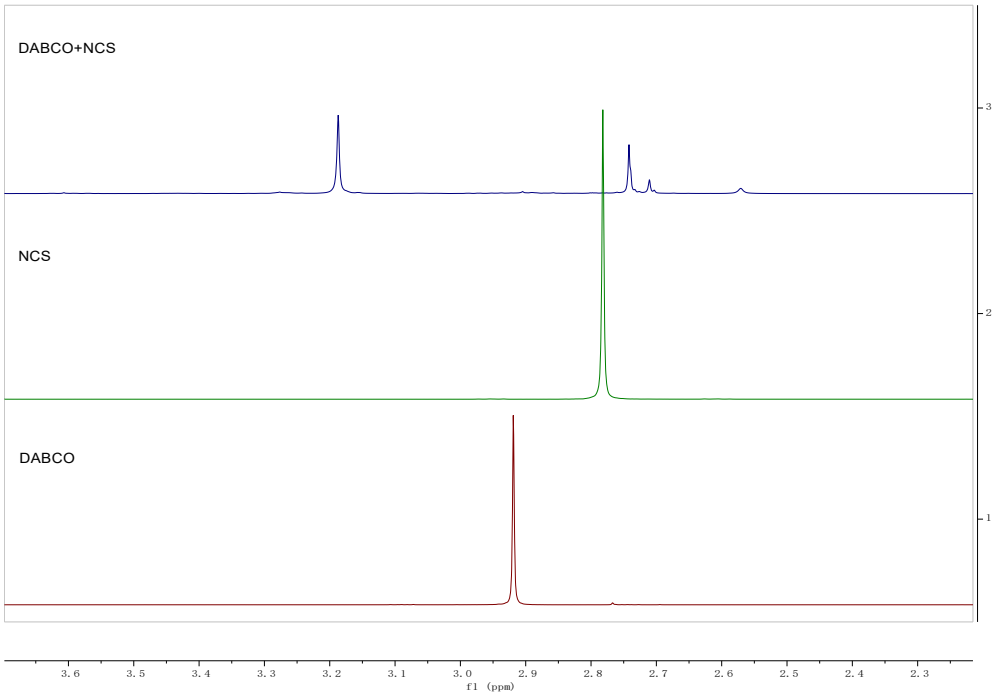
2-Bromo-4-chloro-1,3,5-trimethoxybenzene (2y) [6]



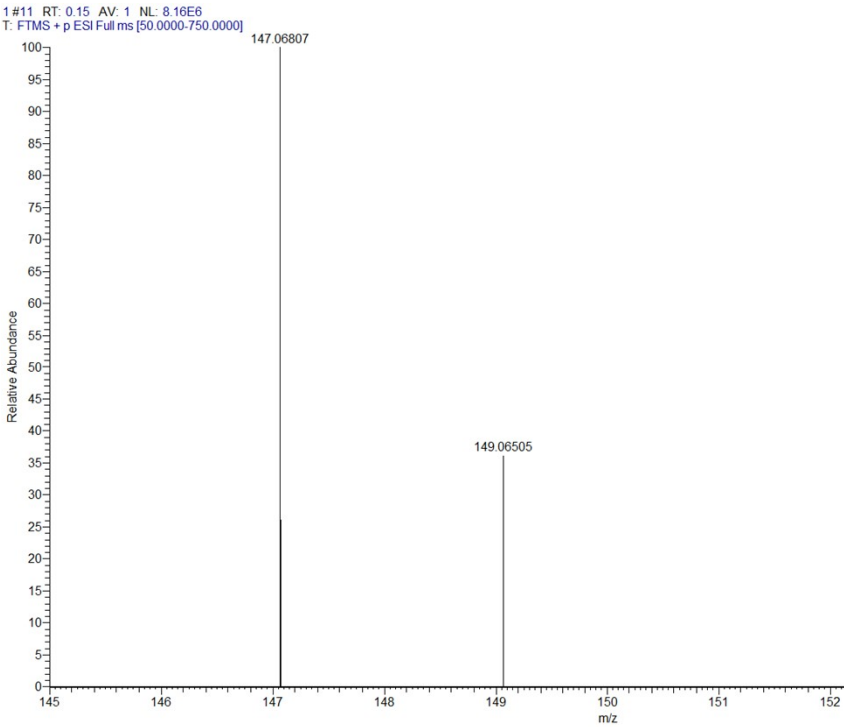
Yield: 92%, white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.37 (s, 1H), 3.92 (s, 3H), 3.91 (s, 3H), 3.88 (s, 3H).

The intermediate tests

1) The NMR spectra (DABCO, NCS and the mixture of DABCO and NCS) indicated the interaction of DABCO and NCS.



2) The peak of DABCO•Cl^+ was detected [HRMS (ESI) Calcd for $(C_6H_{12}ClN_2)^+$: 147.0684, Found: 147.0681].



References

[1] S. Song, X. Li, J. Wei, W. Wang, Y. Zhang, L. Ai, Y. Zhu, X. Shi, X. Zhang, N. Jiao, *Nat. Catal.* **2019**, *3*, 107-115.

[2] Y. Z. Ji, H. J. Li, Y. R. Wang, Z. Y. Zhang, Y. C. Wu, *Adv. Synth. Catal.* **2020**, *362*, 1039-1045.

[3] K. R. Reddy, S. Sana, K. Uppalaiah, K. C. Rajanna, P. Veerasomaiah, *Int. J. Org. Chem.* **2012**, *02*, 254-261.

[4] L. Lu, Y. Li, X. Jiang, *Green Chem.* **2020**, *22*, 5989-5994.

[5] D. A. Rogers, J. M. Gallegos, M. D. Hopkins, A. A. Lignieres, A. K. Pitzel, A. A. Lamar, *Tetrahedron* **2019**, *75*.

[6] R. C. Samanta, H. Yamamoto, *Chem. Eur. J.* **2015**, *21*, 11976-11979.

[7] K. Z. Łączkowski, D. García, D. Peña, A. Cobas, D. Pérez, E. Guitián, *Org. Lett.* **2011**, *13*, 960-963.

[8] A. Granados, A. Shafir, A. Arrieta, F. P. Cossio, A. Vallribera, *J. Org. Chem.* **2020**, *85*, 2142-2150.

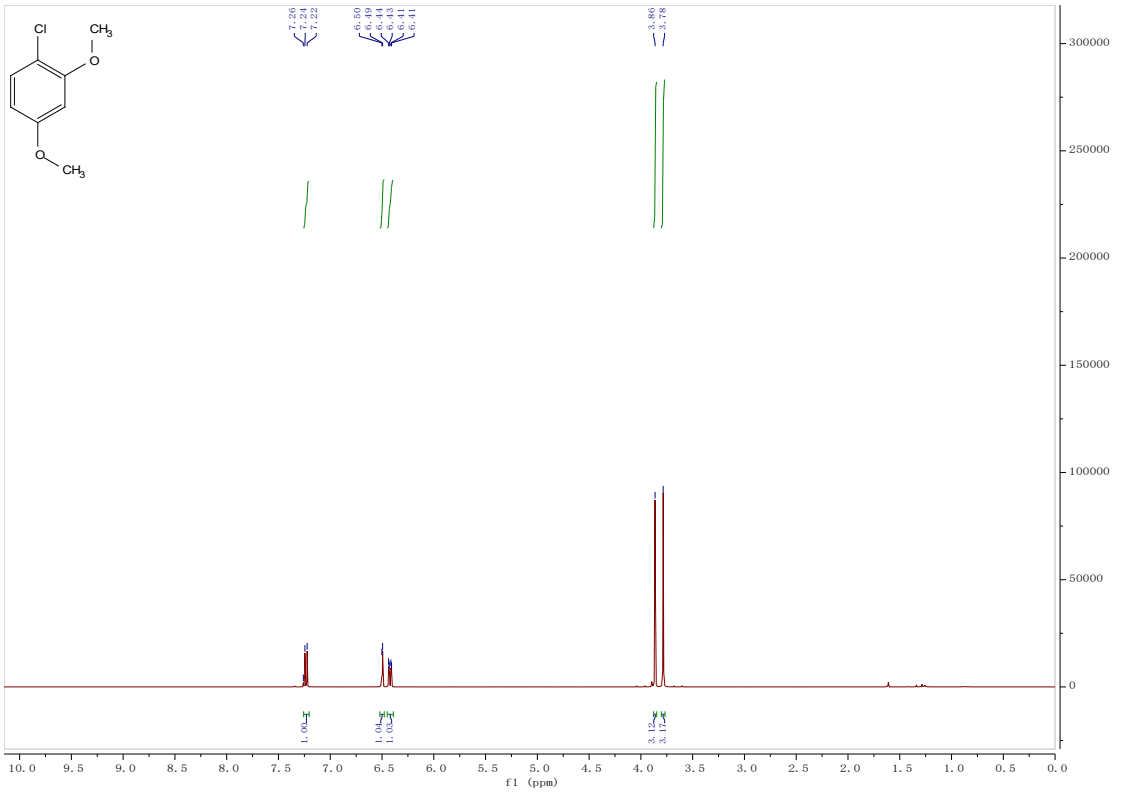
[9] S. Song, X. Sun, X. Li, Y. Yuan, N. Jiao, *Org. Lett.* **2015**, *17*, 2886-2889.

[10] L. T. Ball, G. C. Lloyd-Jones, C. A. Russell, *J. Am. Chem. Soc.* **2014**, *136*, 254-264.

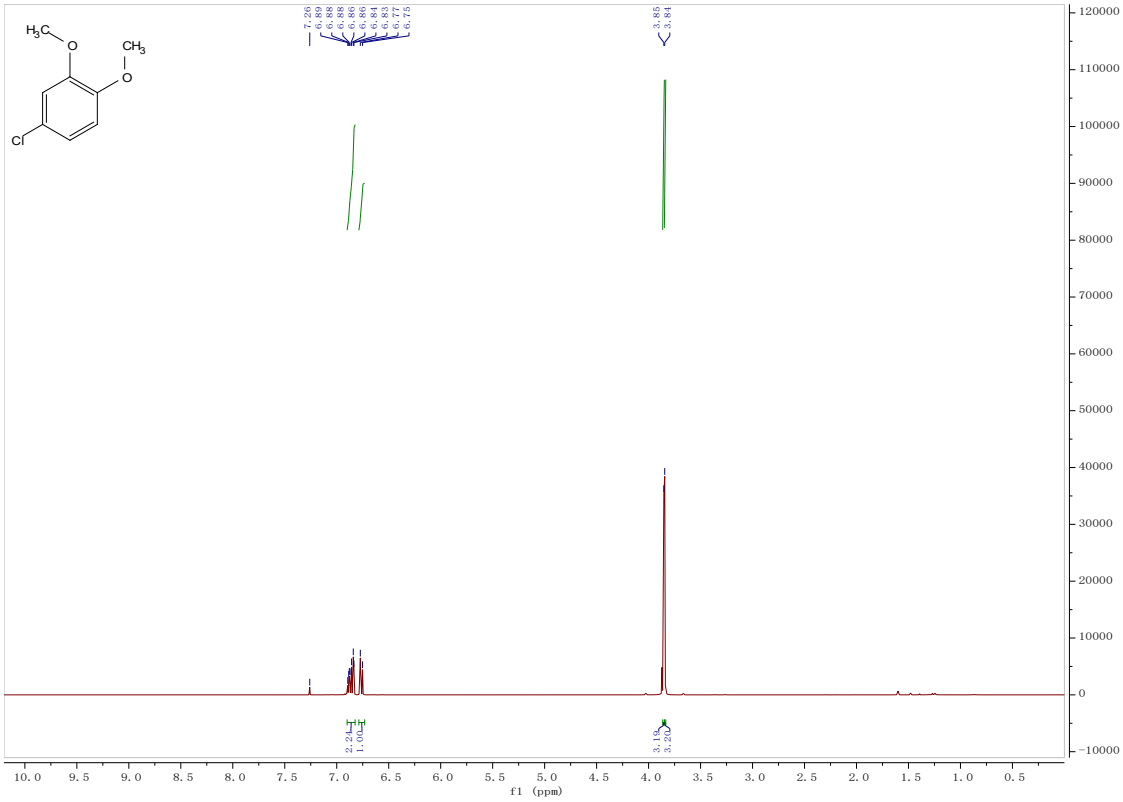
[11] Y. Shi, Z. Ke, Y.-Y. Yeung, *Green Chem.* **2018**, *20*, 4448-4452.

Copies of NMR spectra

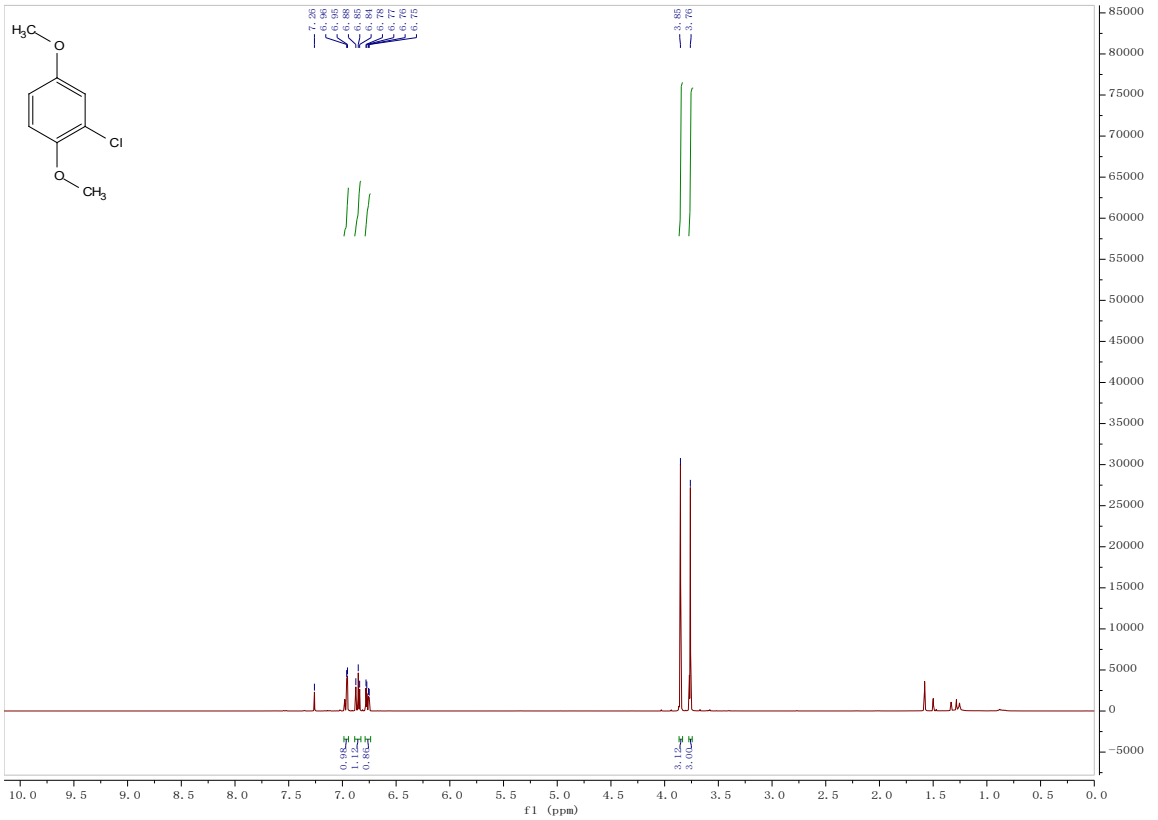
1-Chloro-2,4-dimethoxybenzene (2a)



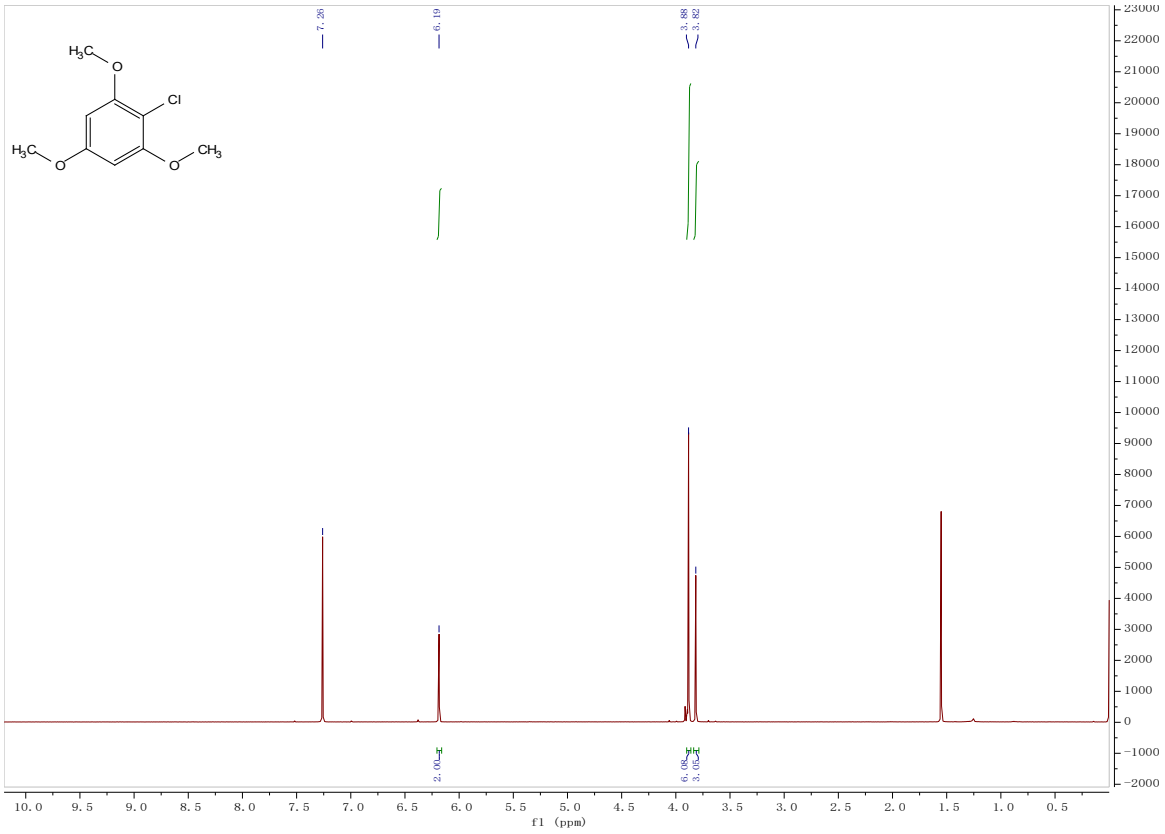
4-Chloro-1,2-dimethoxybenzene (2b)



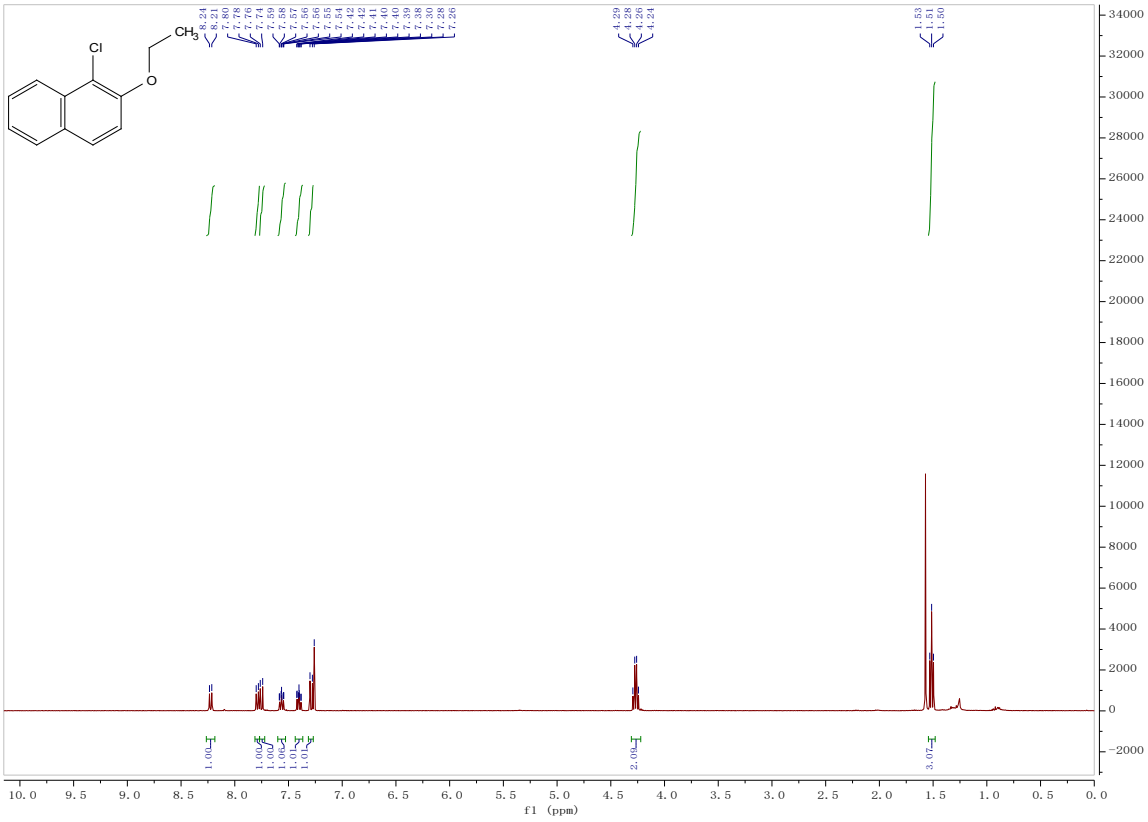
2-Chloro-1,4-dimethoxybenzene (2c)



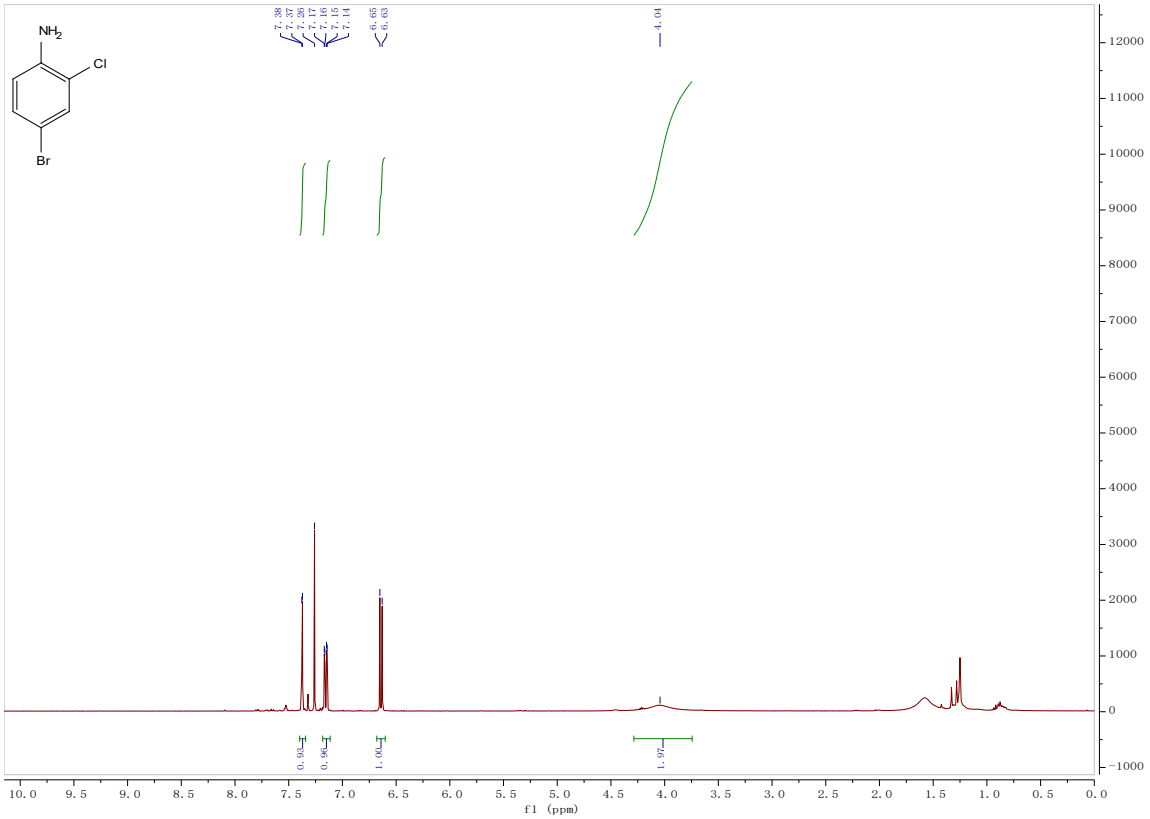
2-Chloro-1,3,5-trimethoxybenzene (2d)



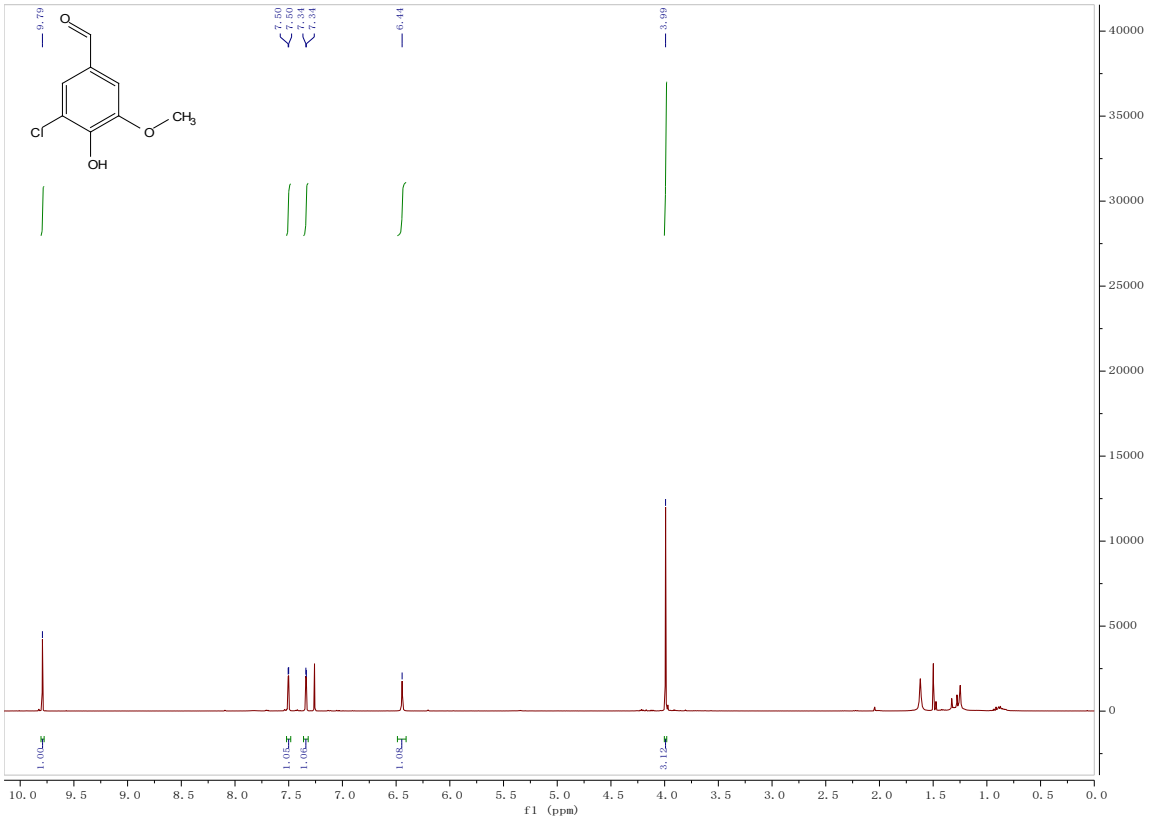
1-Chloro-2-ethoxynaphthalene (2e)



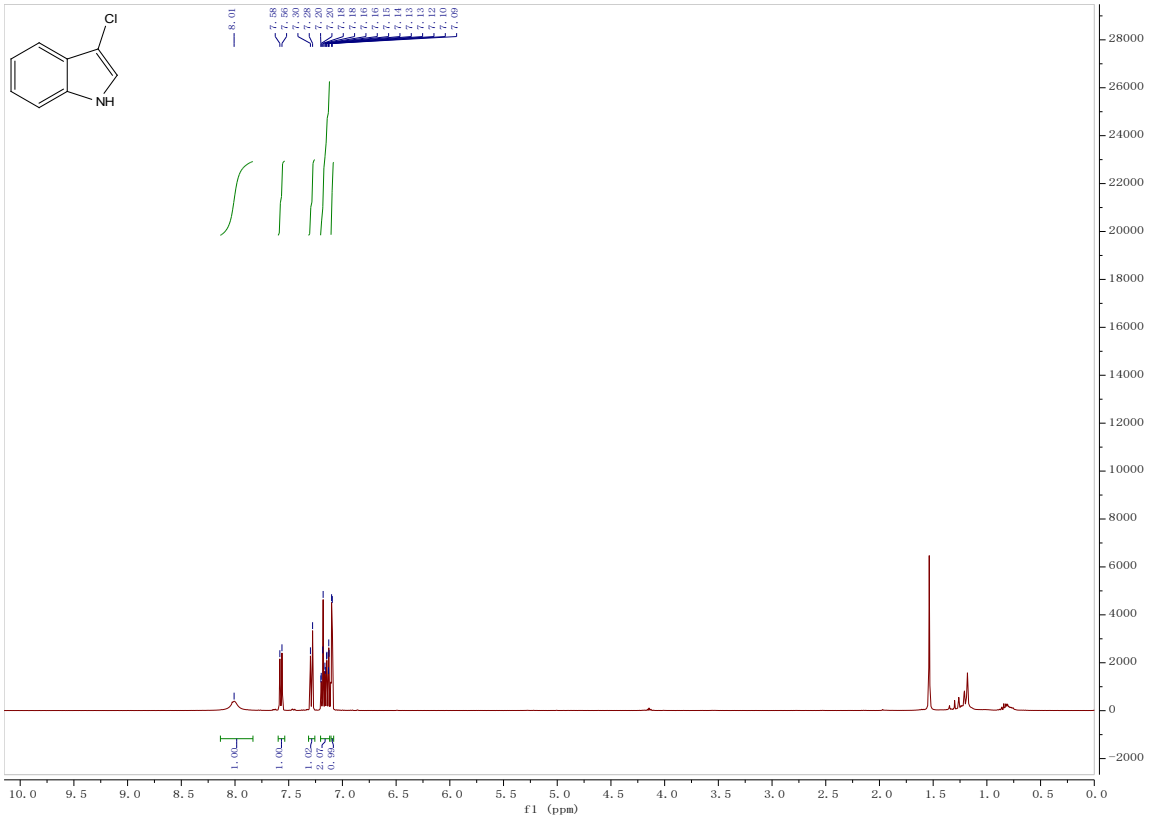
4-Bromo-2-chloroaniline (2f)



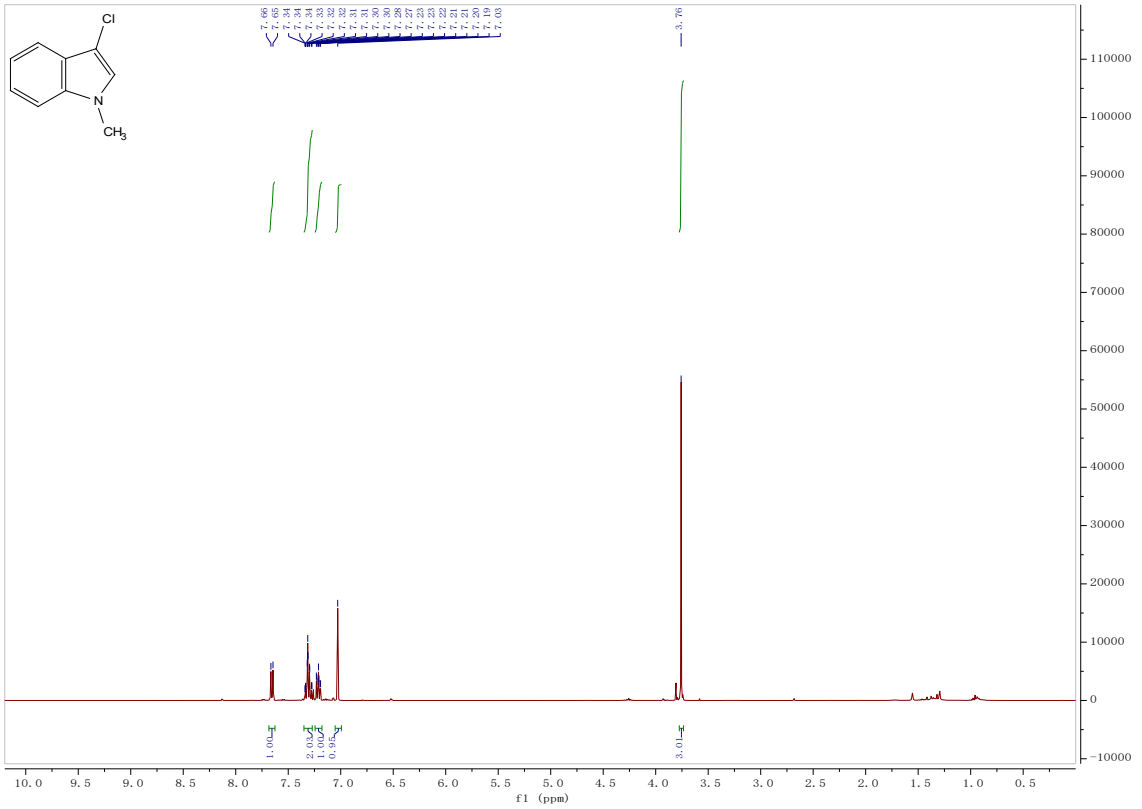
3-Chloro-4-hydroxy-5-methoxybenzaldehyde (2g)



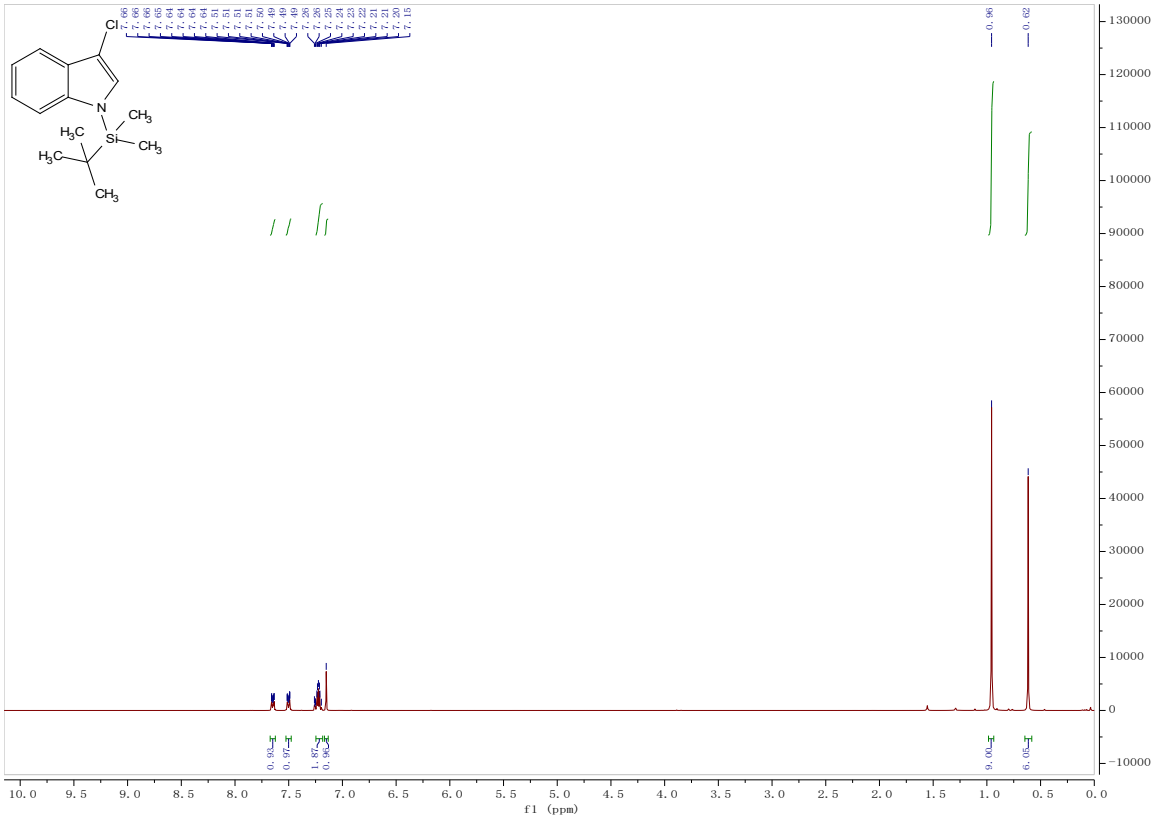
3-Chloro-1H-indole (2j)



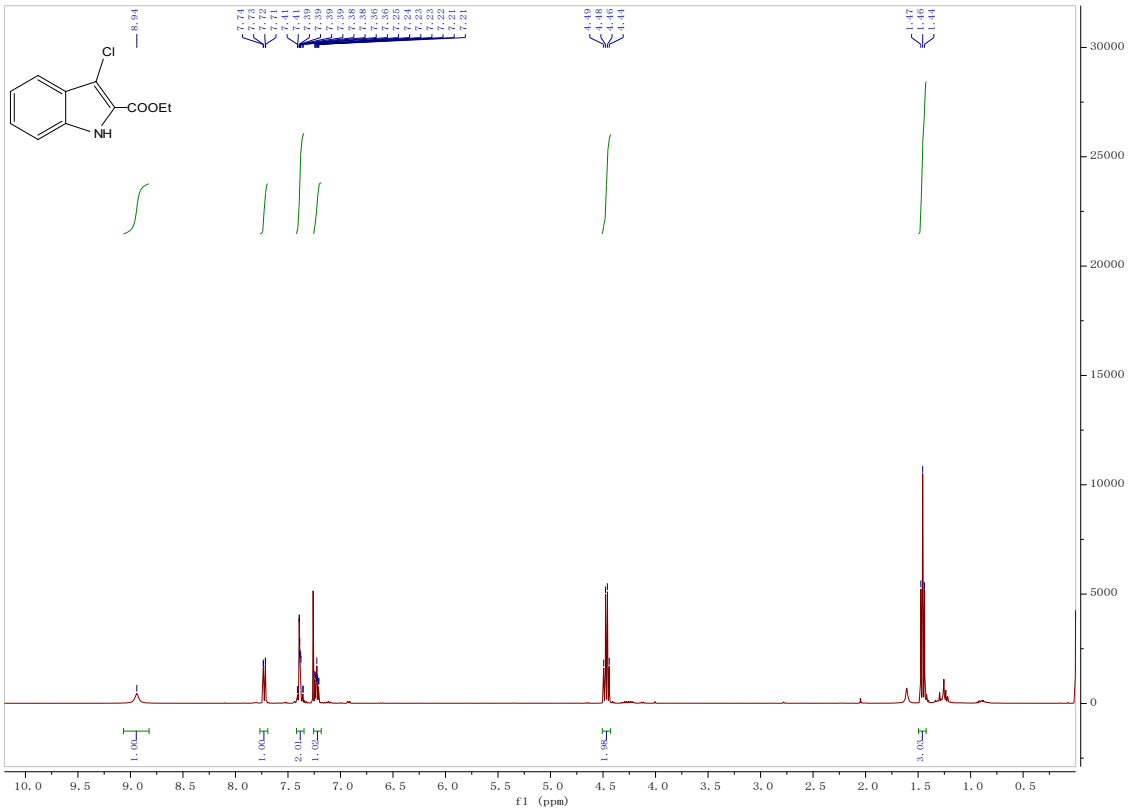
3-Chloro-1-methyl-1H-indole (2k)



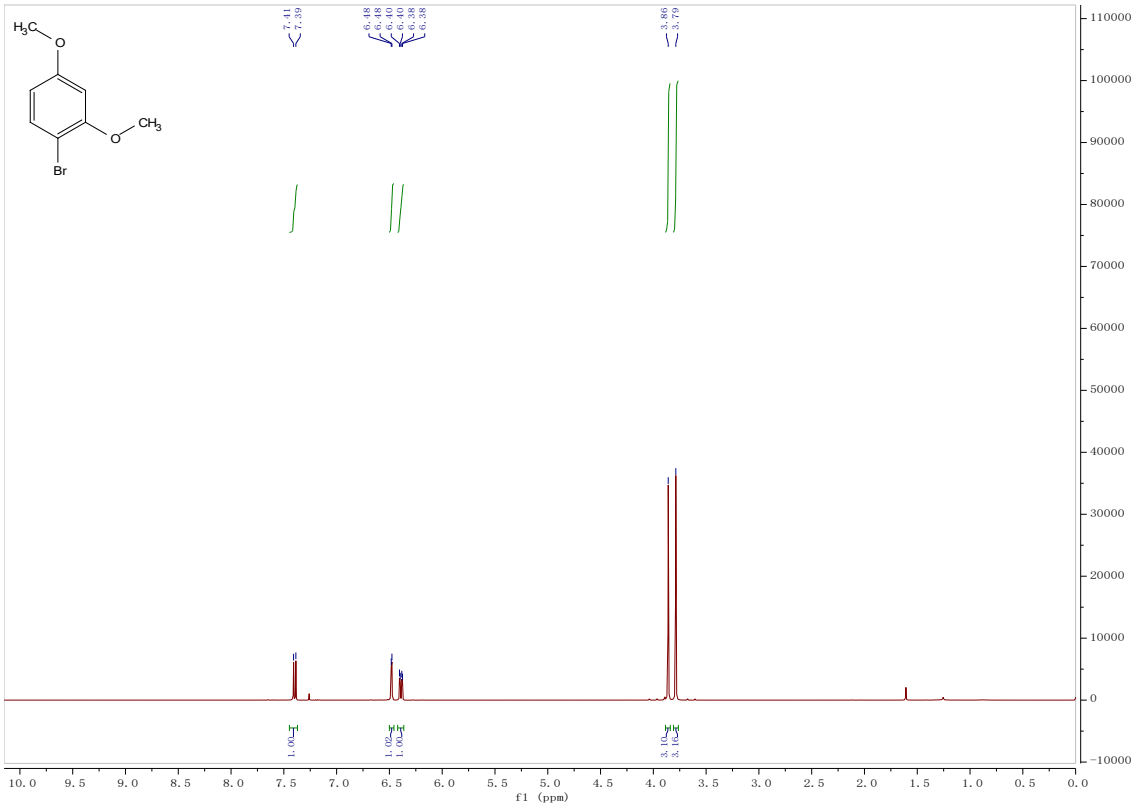
1-(ᵗButyldimethylsilyl)-3-chloro-1H-indole (2l)



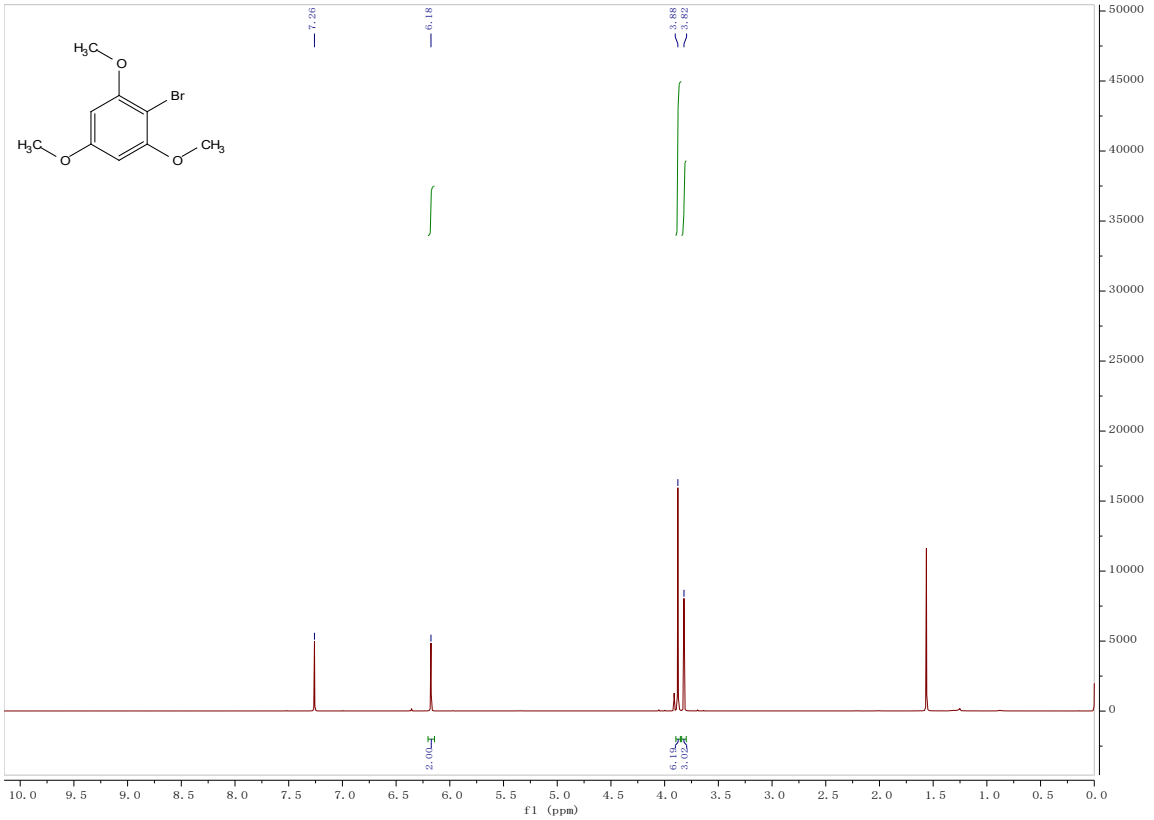
Ethyl 3-chloro-1H-indole-2-carboxylate (2m)



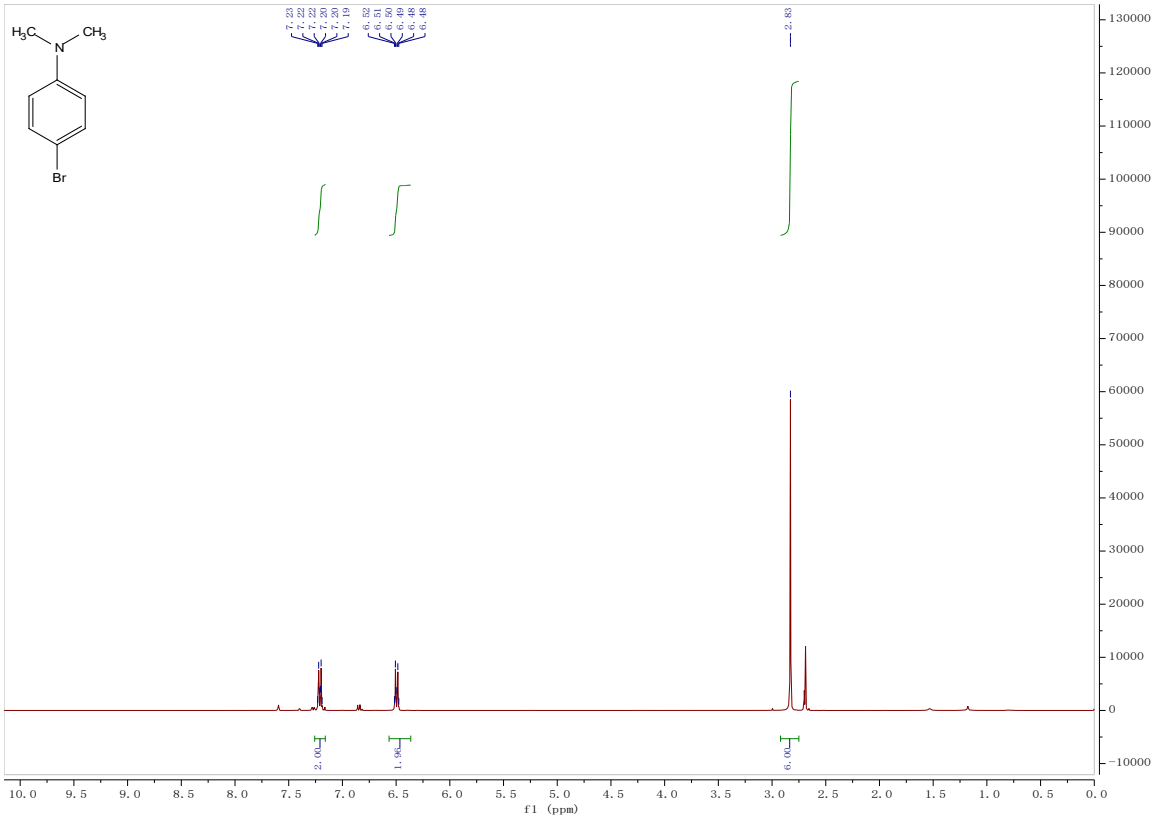
1-Bromo-2,4-dimethoxybenzene (2n)



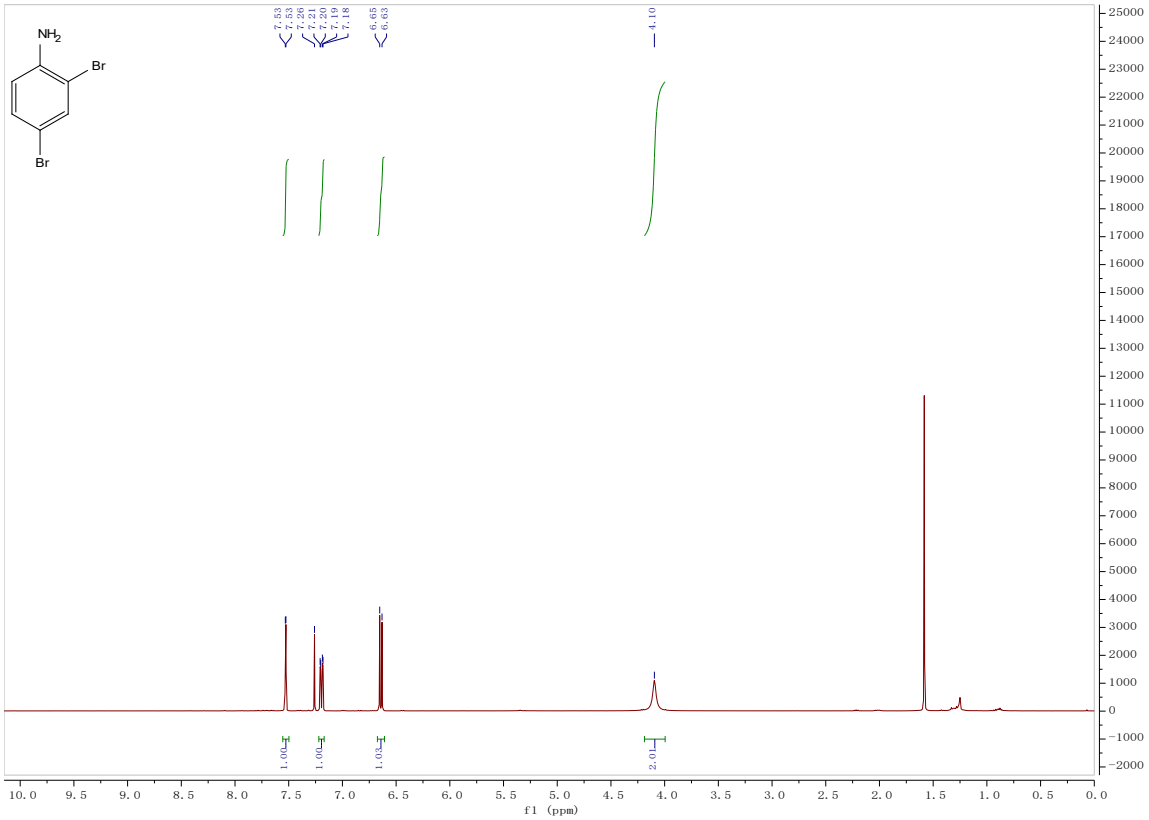
2-Bromo-1,3,5-trimethoxybenzene (2o)



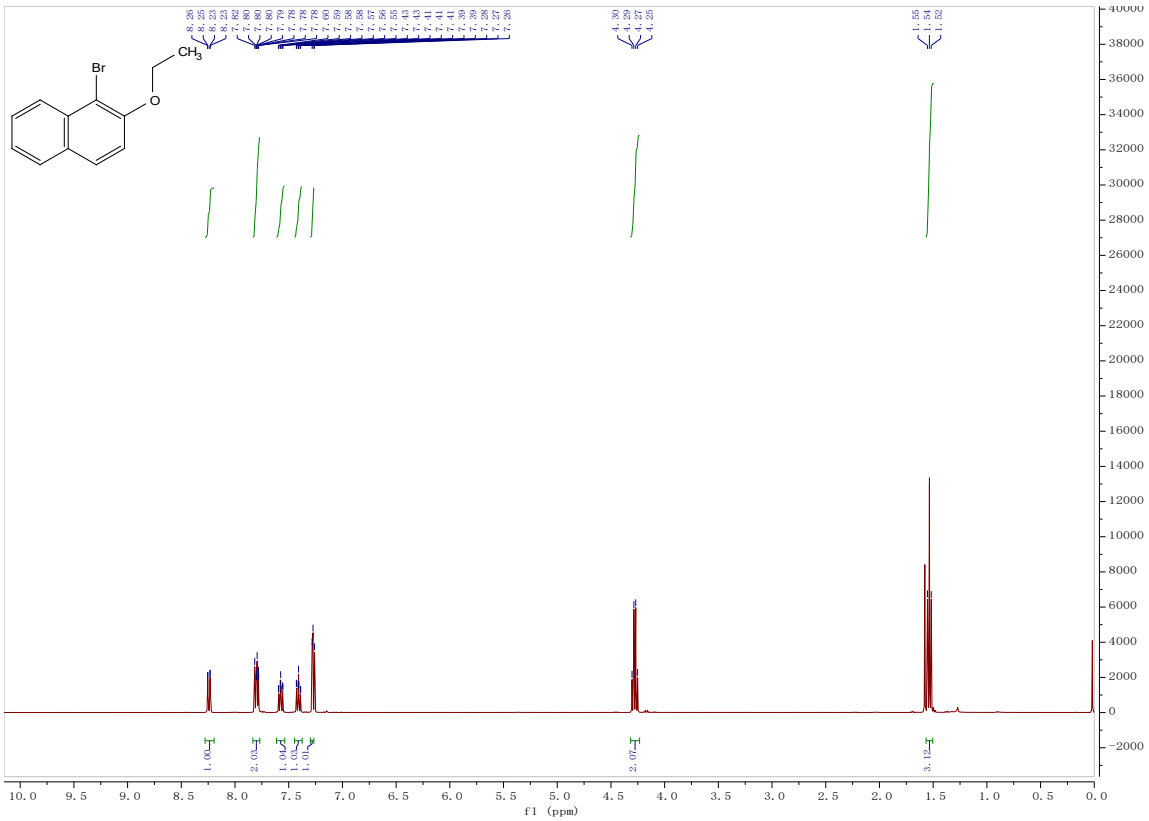
4-Bromo-N,N-dimethylaniline (2p)



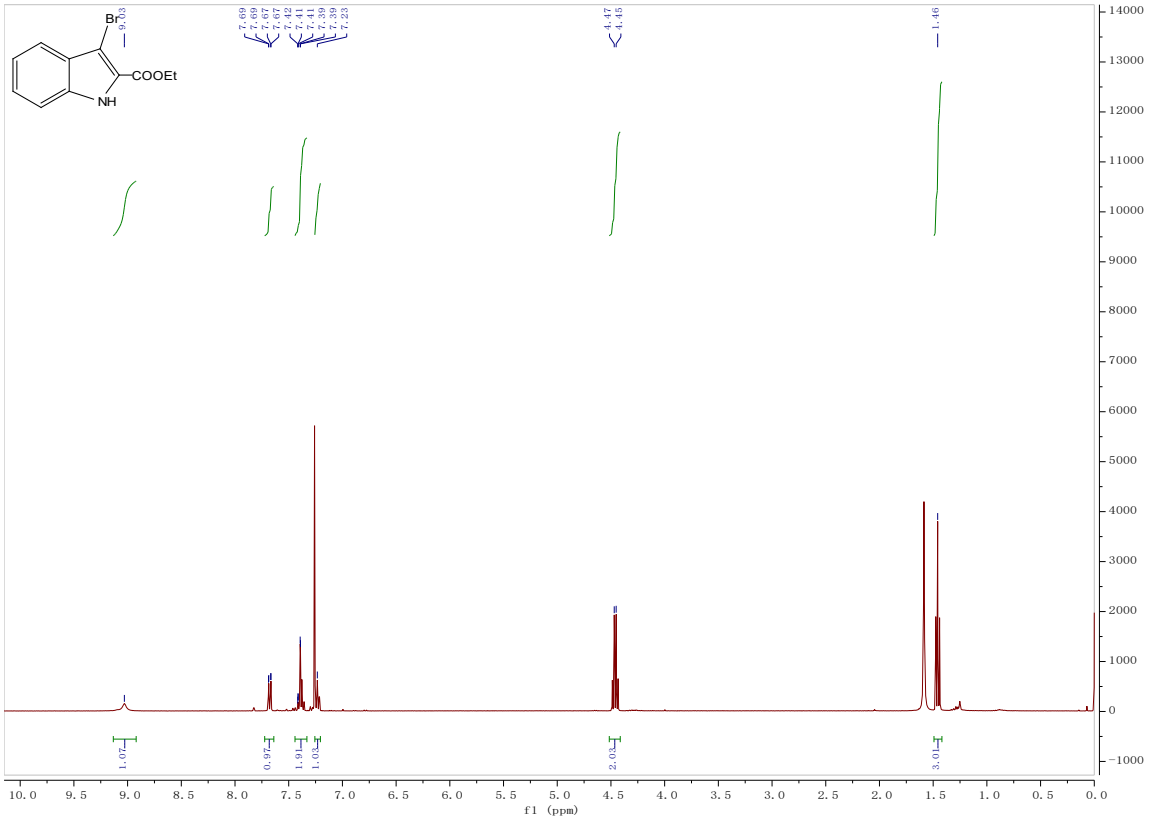
2,4-Dibromoaniline (2q)



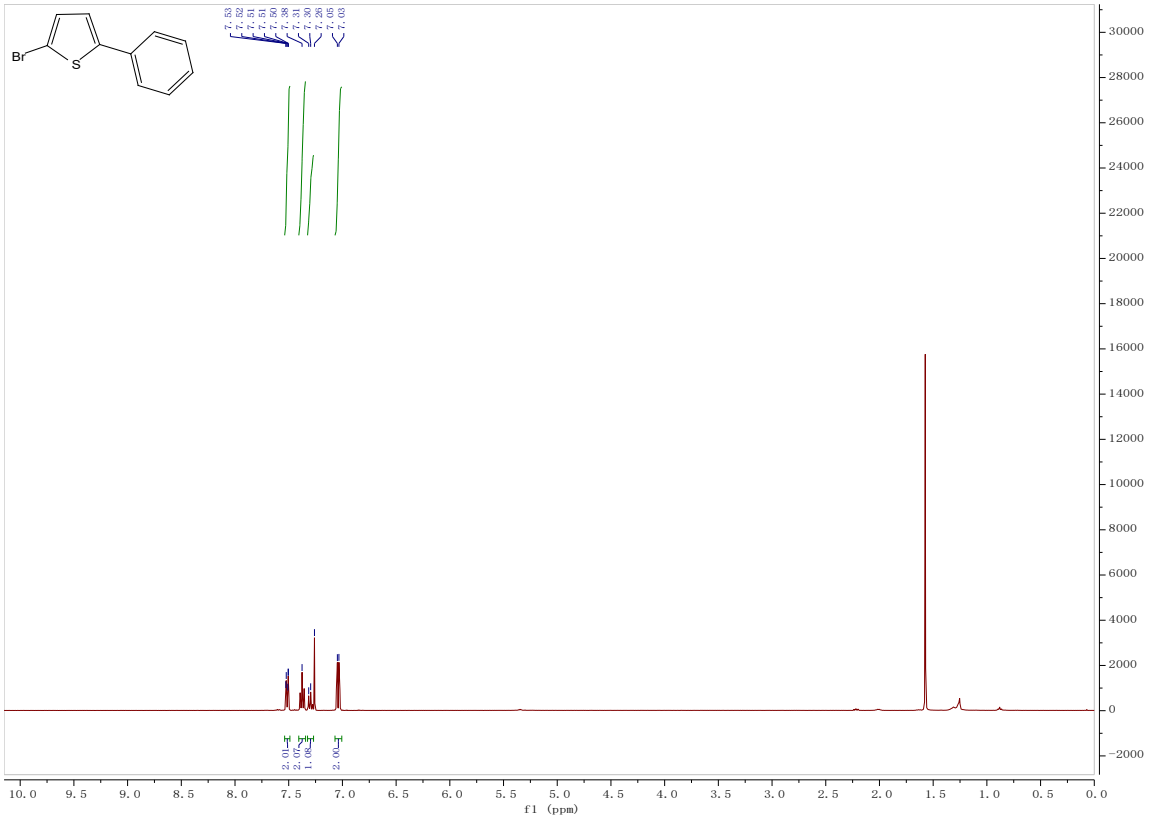
1-Bromo-2-ethoxynaphthalene (2r)



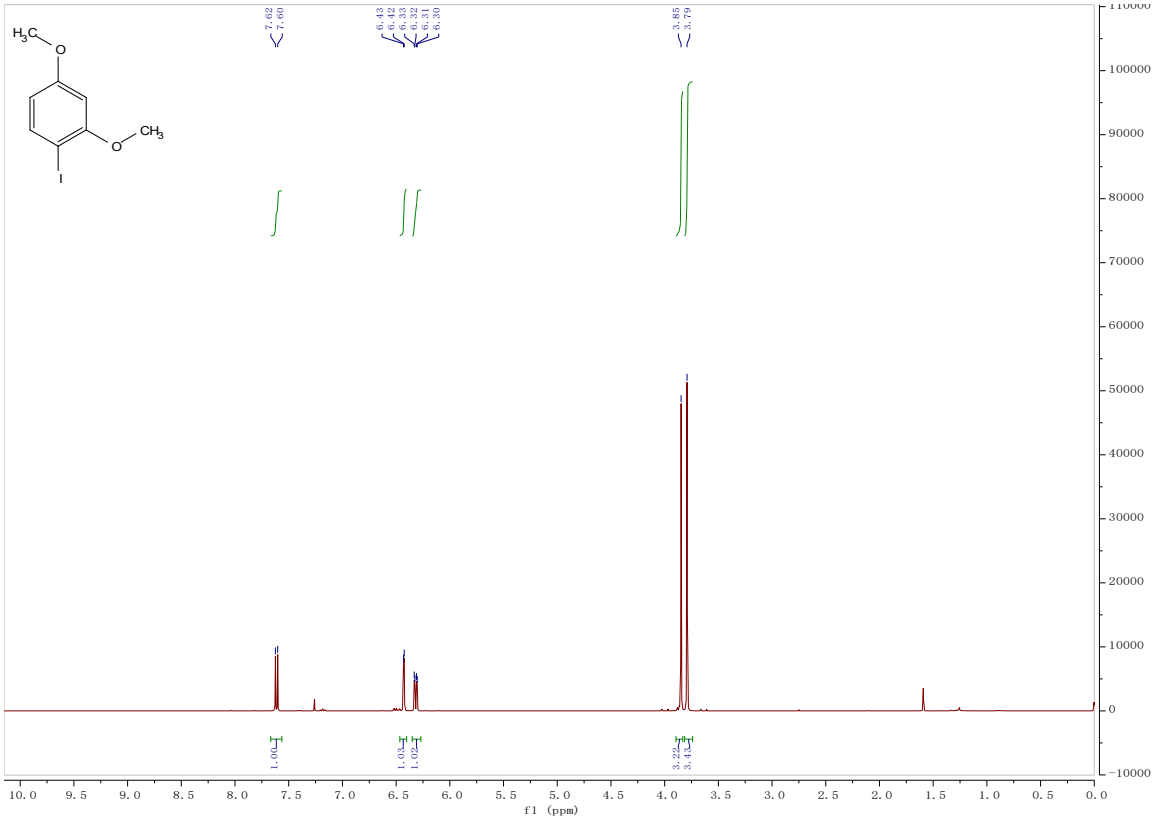
Ethyl 3-bromo-1H-indole-2-carboxylate (2s)



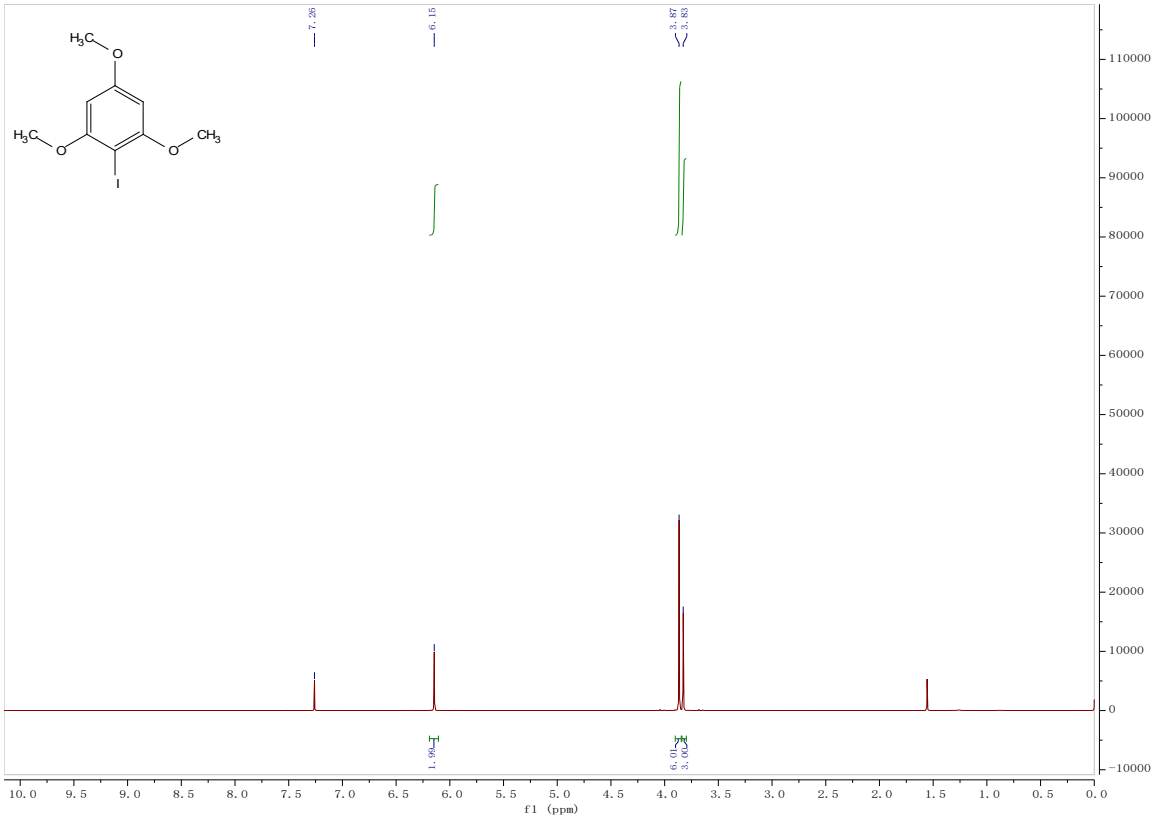
2-Bromo-5-phenylthiophene (2t)



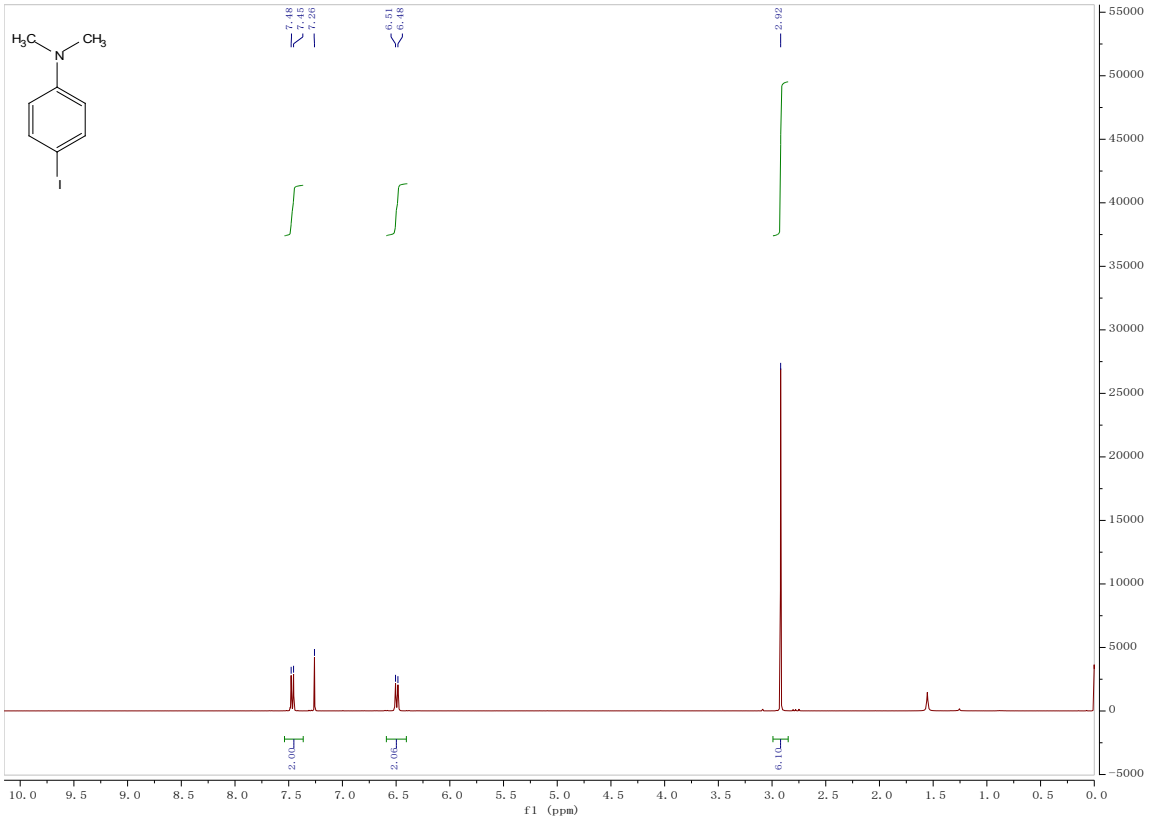
1-Iodo-2,4-dimethoxybenzene (2u)



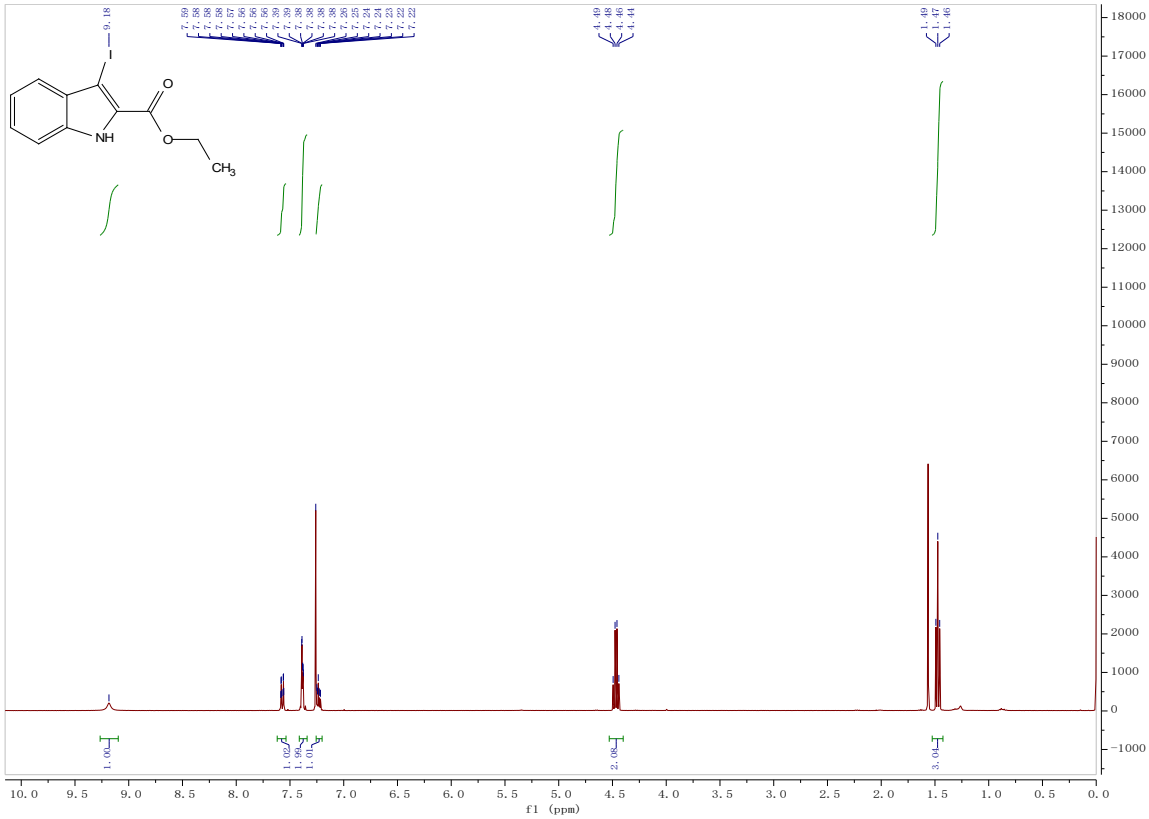
2-Iodo-1,3,5-trimethoxybenzene (2v)



4-Iodo-N,N-dimethylaniline (2w)



Ethyl 3-iodo-1H-indole-2-carboxylate (2x)



2-Bromo-4-chloro-1,3,5-trimethoxybenzene (2y)